OUTLINE OF THE INVENTION

1. A method for generating and analyzing multi-factorial biological response profiles, comprising

a) exposing each member of a plurality of expression control sequences, each of which is operatively linked to a heterologous reporter sequence, independently, to at least about three stimuli from a first set of stimuli, wherein at least about two (*e.g.*, at least about three) of the stimuli in said first set of stimuli are, optionally, combined in an intra-set combinatorial fashion,

b) detecting a first category of responses of said expression control sequences to said stimuli, and

c) generating a response profile for each of said expression control sequences.

2. The method of paragraph 1, wherein at least about two (*e.g.*, at least about three) of the stimuli in said first set of stimuli are combined in an intra-set combinatorial fashion.

3. The method of paragraph 1, further comprising

d) exposing each of said members of the plurality of expression control sequences, independently, to one or more additional sets of stimuli, optionally wherein at least about two (*e.g.*, at least about three) of the stimuli in each of said additional sets of stimuli are combined in an intra-set combinatorial fashion,

in an inter-set combinatorial fashion with set first set of stimuli,

e) detecting the first category of responses of said expression control sequences to the stimuli in d), and

f) generating a response profile for each of said expression control sequences, which includes the responses detected in b) and in e).

4. The method of paragraph 3, wherein at least about two (*e.g.*, at least about three) of the stimuli in each of said additional sets of stimuli are combined in an intra-set combinatorial fashion.

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5. The method of paragraph 3, wherein said members of the plurality of expression control sequences are exposed, independently, to one additional set of stimuli.

6. The method of paragraphs 1 or 3, further comprising detecting one or more different categories of responses of said expression control sequences in a) to said stimuli, and combining those responses with the responses detected in b) and/or in e) to generate a response profile for each of 1, 3, or 6 said expression control sequences.

7. The method of paragraph 1, 3, or 6, wherein the response of the expression control sequences to the stimuli is one or more of the following categories:

    a) levels of RNA produced in response to the stimuli,

    b) levels of proteins translated from said RNA,

    c) levels of post-translational protein modification,

    d) movement of an RNA polymerase molecule along a DNA template (as determined by nuclear run-on analysis) in response to the stimuli, and/or

    e) the formation of protein-DNA complexes (as determined by kinetic analysis) in response to the stimuli, and/or

    f) changes in lipid membrane composition,

    h) or a combination thereof.

8. The method of paragraph 7, further wherein the response of the expression control sequences to the stimuli is

    i) responses detected at one or more different time points following the exposure of each of said expression control sequences to one of more of the stimuli in a) through h), and/or

    j) responses to one or more different amounts (concentrations) or one of more of the stimuli.

9. The method of paragraph 3, wherein the stimuli in the first set and the stimuli in each of the additional sets represent different categories of stimuli.

10. The method of paragraph 9, wherein the different categories are:

a) agents that act at the surface of a cell vs. agents that function within a cell,

b) agents that exhibit different mechanisms of action,

c) agents that have different chemical structures vs. agents within a particular chemical class that differ from one another,

d) agents that are produced within a cell vs. agents that are introduced directly into a cell,

e) agents having a known mechanism of action on an expression control sequence vs. agents not having a known mechanism,

f) agents having a known effect on the expression control sequence vs. test agents,

g) agents known to have an effect on at least one of the expression control sequences vs. agents not known to have an effect on any of those expression control sequences,

h) naturally occurring agents vs. artificially generated molecules, and/or

i) physical agents vs. environmental stimuli, or

j) a combination thereof.

11. The method of paragraph 1, 3, or 6, wherein the response profiles are raw profiles, and generating the raw profiles comprises inputting the responses into a database, thereby generating a database which comprises a raw profile for each of the expression control sequences.

12. The method of paragraph 1, 3, or 6, wherein the response profiles are processed profiles, and generating the processed profiles comprises

inputting the responses into a database, thereby generating a database which comprises a raw profile for each of the expression control sequences, and

processing the data base comprising the raw profiles with a multivariate statistical method.

13. The method of paragraph 12, wherein the multivariate statistical method is

i) principal component analysis,

ii) hierarchical clustering,

iii) unsupervised neural networks, and/or

iv) ANOVA studies,

or a combination thereof.

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14. The method of paragraph 12, wherein the responses are inputted into a computer.

15. The method of paragraph 12, further comprising displaying the processed profiles.

10   16. The method of paragraph 1, 3, or 6, which is a high throughput method.

17. The method of paragraph 1, 3, or 6, wherein at least one of the processes is performed robotically.

15   18. A method of paragraph 1, 3, or 6, which is

a) a method for determining the type of an unknown stimulus (*e.g.*, drug or other agent, environmental effect, etc.),

b) a method for identifying/characterizing a modulatory or co-modulatory agent,

c) a method for identifying the cellular pathway affected by an agent (*e.g.*, a

20   growth factor etc. or a drug),

d) a method for determining whether a drug candidate has an activity similar to a known drug, (or for determining whether a first agent and a second agent act on a cell(s) by a related mechanism of action; dose response, etc.)

e) a method for identifying a regulatory pathway, control point or therapeutic

25   target,

f) a method for studying a combinatorial drug strategy in a pre-clinical setting,

g) a method for identifying a cell or organism that is sensitive or resistant to a drug composition,

h) a method for determining if a sample is susceptible to, or likely to benefit from,

30   a particular treatment, or

i) a method for determining if an agent is toxic.

19. The method of paragraph 1, 3, or 6, wherein each expression control sequence is introduced into a cell by transfection, infection via a viral vector, a gene gun, liposome-mediated delivery, receptor-mediated uptake, or electroporation.

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20. The method of paragraph 19, wherein one or more (preferably, all) of the expression control sequences are introduced into the cell by electroporation.

21. The method of paragraph 1, 3, or 6, wherein the plurality of expression control

10   sequences exhibit coordinated biological activity.

22. The method of paragraph 21, wherein the coordinated biological activity is apoptosis, DNA repair, angiogenesis, signal transduction, vascular invasion, cell growth, reproduction, division, motility, differentiation (including differentiation of a stem cell

15   into a particular type of differentiated cell), activation, or other cellular responses (any of which can be studied in any cell type of interest) T-cell activation, neurogenesis or nerve regeneration, or myogenesis or muscle regeneration.

23. The method of paragraph 1, 3, or 6, wherein the stimuli are physical agents.

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24. The method of paragraph 1, 3, or 6, wherein the stimuli are chemical agents, biological agents, and/or environmental stimuli.

25. The method of paragraph 1, 3, or 6, wherein one or more of the stimuli are drugs,

25   putative drugs, agents known to regulate the expression control sequences, and/or toxins.

26. The method of paragraph 1, 3, or 6, wherein one or more of the stimuli are biological agents, and said agents are introduced into the cell by transfection, infection via a viral vector, a gene gun, liposome-mediated delivery, receptor-mediated uptake, or

30   electroporation.

27. The method of paragraph 1, 3, or 6, wherein one or more of the stimuli are agents that act on the surface of the cell or enter the cell without further treatment.

28. The method of paragraph 1, 3, or 6, wherein one or more of the stimuli are
environmental factors (such as heat, light, radiation, etc.).

29. A computer-implemented method for generating and analyzing multi-factorial biological response profiles, comprising

a) exposing each member of a plurality of expression control sequences, each of which is operatively linked to a heterologous expression control sequence, independently, to

at least about three stimuli from a first set of stimuli, wherein at least about two (*e.g.*, at least about three) of the stimuli in said first set of stimuli are combined in an intra-set combinatorial fashion, and to

at least about three stimuli from a second set of stimuli, wherein at least about two of the stimuli in said second set of stimuli are optionally combined in an intra-set combinatorial fashion,

in an inter-set combinatorial fashion,

b) detecting and inputting into a computer responses of said expression control sequences to said stimuli, thereby generating a database which comprises a raw profile for each of the expression control sequences,

c) processing the data base comprising the raw profiles with

i) principal component analysis,

ii) hierarchical clustering,

iii) unsupervised neural networks, and/or

v) ANOVA studies,

or a combination thereof, and, optionally,

d) displaying the processed profiles.

30. The method of paragraph 1, 3, or 6, wherein one or more of the expression control sequences serves as a positive control, a negative control, or a normalization control.

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31. The method of paragraph 1, 3, or 6, wherein one or more of the stimuli serves as a positive control, a negative control, or a normalization control.

5 32. A method for generating multi-factorial biological response profiles, comprising generating a response profile for each of a plurality of expression control sequences, each of which is operatively linked to a heterologous expression control sequence, from the detected responses of said expression control sequences to a plurality of stimuli, wherein each of said expression control sequences has been exposed, independently, to

10 at least about three stimuli from a first set of stimuli, wherein at least about two (*e.g.*, at least about three) of the stimuli in said first set of stimuli are combined in an intra-set combinatorial fashion, and to

at least about three stimuli from a second set of stimuli, wherein at least about two of the stimuli in said second set of stimuli are optionally combined in an intra-set

15 combinatorial fashion,

in an inter-set combinatorial fashion.

33. A method for generating multi-factorial biological response profiles, comprising processing, with a multivariate statistical method, multi-factorial biological response

20 profiles, which have been obtained by generating a response profile for each of a plurality of expression control sequences, each of which is operatively linked to a heterologous expression control sequence, from the detected responses of said expression control sequences to a plurality of stimuli, wherein each of said expression control sequences has been exposed, independently, to

25 at least about three stimuli from a first set of stimuli, wherein at least about two (*e.g.*, at least about three) of the stimuli in said first set of stimuli are combined in an intra-set combinatorial fashion, and to

at least about three stimuli from a second set of stimuli, wherein at least about two of the stimuli in said second set of stimuli are optionally combined in an intra-set

30 combinatorial fashion,

in an inter-set combinatorial fashion.

34. A method for displaying processed biological response profiles, comprising displaying multi-factorial biological response profiles which have been processed with a multivariate statistical method, wherein the multi-factorial biological response profiles

5 have been obtained by generating a response profile for each of a plurality of expression control sequences, each of which is operatively linked to a heterologous expression control sequence, from the detected responses of said expression control sequences to a plurality of stimuli, wherein each of said expression control sequences has been exposed, independently, to

10   at least about three stimuli from a first set of stimuli, wherein at least about two (*e.g.*, at least about three) of the stimuli in said first set of stimuli are combined in an intra-set combinatorial fashion, and to

     at least about three stimuli from a second set of stimuli, wherein at least about two of the stimuli in said second set of stimuli are optionally combined in an intra-set

15 combinatorial fashion,

     in an inter-set combinatorial fashion.

35. A kit, comprising

     (1) a plurality of [*e.g.*, at least about 3] recombinant constructs, each of which

20 comprises an expression control sequence from a coordinated system of interest operatively linked to a reporter,

     (2) at least three about agents from a first set of agents that are known or predicted to act on at least one of said expression control sequences, and

     (3) at least about three agents from a second set of agents,

25   wherein said at least about three agents from said first and second sets of agents are combined in an inter-set combinatorial fashion

     and, optionally,

     (3) an electroporation device suitable for electroporating said recombinant constructs into suitable cells; and/or

30   (4) instructions for how to detect the effects of the agents on the expression control sequences.

36. The kit of paragraph 35, wherein

a) the expression control sequences regulate genes from a signal transduction pathway,

5   b) the first set of agents comprises mitogens, growth factors, and/or hormones that act on the expression control sequences of a), and

c) the second set of agents comprises pharmaceutical agents.

37. The kit of paragraph 36, wherein

10   a) the expression control sequences are one or more of those listed in column 1 of Table. 1 (Table 1, from, IL-2, CD28RE-TRE, NFAT, AP-1, NFkB, CREB, UAS/p300 N-term, UAS/p300 FL), Smad binding sites, Stat (1-6) binding sites, SP-1 binding sites, c-myc binding sites, ets binding sites, ATF-2 bindings sites, C/EBP binding sites, HIV-LTR, MMTV-LTR, HTLV-1-LTR, Erg-1 binding sites; gamma interferon

15   activated sequence (GAS), GATA 1-3 binding sites, Oct-1,2 binding sites, LMO-1,2, P53 binding site, E2F-1,2 binding sites, ZBP 89 binding sites, or HSV-8 promoter),

b) the first set of agents comprises one more of the agents in column 2 of Table 1, testosterone and analogues, estrogen and analogues, insulin, EGF (epidermal growth factor, NGF (nerve growth factors), Interleukins (1-15), Rantes family, TNF family

20   (tumor necrosis factor), adrenalin, corticosteroids, human growth hormone, anabolic steroids, progestins, prolactin, thyroid hormones, pituitary hormones, parathyroid hormones, vaso-intestinal peptide, gastrin, all forms of (CSF's) colony stimulating factors, or all forms of oral contraceptives, and

c) the second set of agents comprises one or more of the agents in column 3 of

25   Table 1; the immunomodulatory agents FK506, Pentoxfiline, Methotrexate, Dexamethasone, or rapamycin; or the following pharmacological agents, all of which modify cellular signaling pathways: anti-diarrheals, anti-hypertenson, anti-histamines, narcotic agents, anti-anxiolytic agents, anti-depressants, anti-metabolite agents, including over the counter drugs, herbal remedies, all oral and intravenous chemotherapeutic

30   agents, new line chemotherapeutic agents, anti-angiogenesis agents, histone deacetylase

inhibitors, active ingredients in food, caffeine, MSG (mono-sodium glutamate), or all viral gene therapy agents including empty viral vectors.

38. A method for generating multi-factorial biological response profiles, comprising

5   a) exposing each member of a plurality of expression control sequences, each of which is from a signal transduction gene, and/or is from a gene that is responsive to a signal transduction protein, independently, to

at least about three stimuli from a first set of agents known to have an effect on the expression control sequences, wherein at least two (*e.g.*, at least about three)

10   of the stimuli in the first set are combined in an intra-set combinatorial fashion, and to

at least about three stimuli from a second set of agents, wherein at least two (*e.g.*, at least about three) of the stimuli in the second set are optionally combined in an intra-set combinatorial fashion,

in an inter-set combinatorial fashion,

15   wherein each of the expression control sequences is operatively linked to a heterologous reporter in a recombinant construct, and

wherein each of the recombinant constructs is introduced into a cell that comprises one or more signal transduction genes, or genes that are responsive to signal transduction proteins; and all of the recombinant constructs are introduced into the cells

20   simultaneously,

b) detecting the responses of said expression control sequences to said stimuli, and

c) generating a response profile for each of said expression control sequences.

25   39. The method of paragraph 38, wherein

a) the plurality of expression control sequences comprise one or more of: the sequences listed in Row 1 of Table I (Table 1, from, IL-2, CD28RE-TRE, NFAT, AP-1, NFkB, CREB, UAS/p300 N-term, UAS/p300 FL); Smad binding sites, Stat (1-6) binding sites, SP-1 binding sites, c-myc binding sites, ets binding sites, ATF-2 bindings

30   sites, C/EBP binding sites, HIV-LTR, MMTV-LTR, HTLV-1-LTR, Erg-1 binding sites; Gamma interferon activated sequence (GAS), GATA 1-3 binding sites, Oct-1,2 binding

sites, LMO-1,2, P53 binding site, E2F-1,2 binding sites, ZBP 89 binding sites, or HSV-8 promoter,

b) the stimuli in the first set of agents comprise stimulatory and/or regulatory agents (such as mitogens, growth factors, hormones, or the like), and

5 c) the stimuli in the second set of agents comprise pharmacological agents (such as immunomodulatory agents) that are known or expected to modify cellular signaling pathways.

40. The method of paragraph 39, wherein

10 a) the stimuli in the first set of agents comprise the agents listed in column 2 of Table 1, testosterone and analogues, estrogen and analogues, insulin, EGF (epidermal growth factor, NGF (nerve growth factors), interleukins (1-15), Rantes family, TNF family (tumor necrosis factor), adrenalin, corticosteroids, human growth hormone, anabolic steroids, progestins, prolactin, thyroid hormones, pituitary hormones-

15 parathyroid hormones, vaso-intestinal peptide, gastrin, all forms of (CSF's) colony stimulating factors, or all forms of oral contraceptives, and

b) the stimuli in the second set of agents comprise the agents listed in column 3 of Table 1, FK506, Pentoxfiline, Methotrexate, Dexamethasone, rapamycin; the following immunomodulatory agents: FK506, Pentoxfiline, Methotrexate, Dexamethasone,

20 rapamycin; or the following pharmacological agents, all of which modify cellular signaling pathways: anti-diarrheals, anti-hypertenson, anti-histamines, narcotic agents, anti-anxiolytic agents, anti-depressants, anti-metabolite agents, including over the counter drugs, herbal remedies, all oral and intravenous chemotherapeutic agents, new line chemotherapeutic agents, anti-angiogenesis agents, histone deacetylase inhibitors, active

25 ingredients in food, caffeine, MSG (mono-sodium glutamate), all viral gene therapy agents including empty viral vectors, hallucinogenic drugs, neuroleptics and all sedatives, and

c) the recombinant constructs are electroporated into the cells.

30 41. The method of paragraph 38, further comprising

d) inputting the responses into a computer, thereby generating a database which comprises a raw profile for each of the biological entities,

e) processing the data base comprising the raw profiles with

i) principal component analysis,

ii) hierarchical clustering,

iii) unsupervised neural networks, and/or

v) ANOVA studies,

or a combination thereof, and, optionally,

f) displaying the processed profiles.

42. A computer system for generating and analyzing multi-factorial biological response profiles, comprising

a) means for inputting responses into a database, wherein said responses are generated by

i) exposing each member of a plurality of expression control sequences, each of which is operatively linked to a heterologous expression control sequence, independently, to

at least about three stimuli from a first set of stimuli, wherein at least two (*e.g.*, at least about three) of the stimuli in said first set of stimuli are combined in an intra-set combinatorial fashion, and to

at least about three stimuli from a second set of stimuli, wherein at least about two of the stimuli in said second set of stimuli are optionally combined in an intra-set combinatorial fashion,

in an inter-set combinatorial fashion, and

ii) detecting the responses of said biological entities to said stimuli;

b) means for analyzing said inputted responses (*e.g.*,for reducing the number of dimensions of said inputted responses to three dimensions); and, optionally,

c) means for displaying the analyzed responses.

43. A computer-readable storage medium storing computer-readable program code for causing a computer to perform the following steps:

a) retrieving responses generated by

   i) exposing each member of a plurality of expression control sequences, each of which is operatively linked to a heterologous expression control sequence, independently, to

   at least about three stimuli from a first set of stimuli, wherein at least two (*e.g.*, at least about three) of the stimuli in said first set of stimuli are combined in an intra-set combinatorial fashion, and to

   at least about three stimuli from a second set of stimuli, wherein at least about two (*e.g.*, at least about three) of the stimuli in said second set of stimuli are optionally combined in an intra-set combinatorial fashion,

   in an inter-set combinatorial fashion, and

   ii) detecting the responses of said biological entities to said stimuli,

b) processing the retrieved responses with a multivariate statistical method and, optionally,

c) displaying the processed responses.

44. The method of paragraph 43, wherein the multivariate statistical method is

   A) principle component analysis,

   B) hierarchical clustering,

   C) unsupervised neural networks, and/or

   D) ANOVA studies,

   or a combination thereof

45. A database (a reference database) of processed profiles, prepared by the method of paragraph 12, suitable to compare results from a different cell line or set of expression control sequences.

46. A reference database of processed profiles, prepared by the method of paragraph 29.

47. A reference database of processed profiles, prepared by the method of paragraph 21.

48. An integrated system for deciphering the inter-relationships of expression control sequences / mechanism of cellular function, and/or transcriptional targeting, comprising

    a) a plurality of expression control sequences, each of which is operatively linked to a heterologous expression control sequence, which have been exposed, independently,

5   to

    at least about three stimuli from a first set of stimuli, wherein at least about two (*e.g.*, at least about three) of the stimuli in said first set of stimuli are combined in an intra-set combinatorial fashion, and to

    at least about three stimuli from a second set of stimuli, wherein at least

10   about two (*e.g.*, at least about three) of the stimuli in said second set of stimuli are optionally combined in an intra-set combinatorial fashion,

    in an inter-set combinatorial fashion,

    b) a detection system for receiving the plurality of expression control sequences, wherein the detection system detects the responses of the expression control sequences to

15   the stimuli, and generates a plurality of data points based upon the responses, and

    c) a data analyzing system in operational communication with the detection system, the data analyzing system comprising a computer or computer-readable medium comprising one or more logical instructions for organizing the plurality of data points into a database and one or more logical instructions for analyzing the plurality of data

20   points.

49. The integrated system of paragraph 48, wherein the detection system detects a signal or a result from an analytical technique.

25   50. The integrated system of paragraph 48, wherein the analytical technique comprises an RNA transcription assay, a protein expression assay, a protein function assay, a phenotype-based cellular assay, a metabolic assay, a cofactor or small molecule assay, an ionic potential-measuring assay, a reporter gene assay, or a combination thereof.

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51. The integrated system of paragraph 48, wherein the detection system detects the at least one response at a plurality of time points.

52. The integrated system of paragraph 48, wherein the detection system detects a plurality of responses at a plurality of time points.

5 53. The integrated system of paragraph 48, wherein the database comprises a plurality of profiles for the plurality of biological entities.

54. The integrated system of paragraph 48, wherein the one or more logical instructions for analyzing the plurality of data points comprises software for generating a

10 graphical representation of the plurality of responses and the plurality of time points.

55. The integrated system of paragraph 48, wherein the one or more logical instructions for analyzing the plurality of data points comprises software for performing multivariate analysis for the plurality of data points.

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56. The integrated system of paragraph 48, wherein the one or more logical instructions for analyzing the plurality of data points comprises software for analyzing the plurality of data points in n-dimensional space.

20 57. The integrated system of paragraph 48, wherein the one or more logical instructions for analyzing the plurality of data points comprises software for performing principle component analysis upon the plurality of data points.

58. The integrated system of paragraph 48, wherein the one or more logical

25 instructions for analyzing the plurality of data points comprises software for performing difference analysis upon the plurality of data points.

59. The integrated system of paragraph 48, further comprising an output file.

30 60. The integrated system of paragraph 59, wherein the output file comprises a network model of the plurality of data.

61. A method for generating multi-factorial biological response profiles, comprising

    a) exposing each member of a plurality of biological entities, independently, to at least about three stimuli from a first set of stimuli, and to at least about three stimuli from a second set of stimuli, in an <u>inter-set</u> combinatorial fashion,

        i) wherein at least about two (*e.g.*, at least about three) members of the stimuli in said first set of stimuli are, optionally, combined in an <u>intra-set</u> combinatorial fashion, but none of the members of the stimuli in the second set of stimuli are combined in an intra-set combinatorial fashion, or

        ii) wherein at least about two (*e.g.*, at least about three) members of the stimuli in said second set of stimuli are, optionally, combined in an <u>intra-set</u> combinatorial fashion, but none of the members of the stimuli in the first set of stimuli are combined in an intra-set combinatorial fashion, or

        iii) wherein

    at least about two (*e.g.*, at least about three) members of the stimuli in said first set of stimuli are, optionally, combined in an <u>intra-set</u> combinatorial fashion, and

    at least about two (*e.g.*, at least about three) members of the stimuli in said second set of stimuli are, optionally, combined in an <u>intra-set</u> combinatorial fashion, and

    the members of the first set and the second set of stimuli represent different categories of stimuli.

    b) detecting the responses of said biological entities to said stimuli, and

    c) generating a response profile for each of said biological entities.

62. The method of paragraph 61, wherein one or more of the biological entities is within a cell and is treated with the stimuli *in vivo*.

63. The method of paragraph 61, wherein each of said biological entities is within a cell and is treated with the stimuli *in vivo*.

64. The method of paragraph 61, wherein one or more of the biological entities is treated with the stimuli *in vitro*.

61. A method for generating multi-factorial biological response profiles, comprising

    a) exposing each member of a plurality of biological entities, independently, to at least about three stimuli from a first set of stimuli, and to at least about three stimuli from a second set of stimuli, in an <u>inter-set</u> combinatorial fashion,

        i) wherein at least about two (*e.g.*, at least about three) members of the stimuli in said first set of stimuli are, optionally, combined in an <u>intra-set</u> combinatorial fashion, but none of the members of the stimuli in the second set of stimuli are combined in an intra-set combinatorial fashion, or

        ii) wherein at least about two (*e.g.*, at least about three) members of the stimuli in said second set of stimuli are, optionally, combined in an <u>intra-set</u> combinatorial fashion, but none of the members of the stimuli in the first set of stimuli are combined in an intra-set combinatorial fashion, or

        iii) wherein

    at least about two (*e.g.*, at least about three) members of the stimuli in said first set of stimuli are, optionally, combined in an <u>intra-set</u> combinatorial fashion, and

    at least about two (*e.g.*, at least about three) members of the stimuli in said second set of stimuli are, optionally, combined in an <u>intra-set</u> combinatorial fashion, and

    the members of the first set and the second set of stimuli represent different categories of stimuli.

    b) detecting the responses of said biological entities to said stimuli, and

    c) generating a response profile for each of said biological entities.

62. The method of paragraph 61, wherein one or more of the biological entities is within a cell and is treated with the stimuli *in vivo*.

63. The method of paragraph 61, wherein each of said biological entities is within a cell and is treated with the stimuli *in vivo*.

64. The method of paragraph 61, wherein one or more of the biological entities is treated with the stimuli *in vitro*.

65. The method of paragraph 61, wherein each of said biological entities is an expression control sequence that is operatively linked to a coding sequence, in a recombinant construct.

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66. The method of paragraph 65, wherein one or more of said coding sequences is a sequence that is naturally under the control of the expression control sequence to which it is operatively linked.

10   67. The method of paragraph 65, wherein one or more of said coding sequences encodes a heterologous reporter.

68. In a nuclear run-on method to characterize mRNA transcription from a genomic DNA
15   template of interest, the improvement comprising hybridizing labeled nascent mRNAs transcribed from said genomic DNA template to an arrangement of at least three addressable oligonucleotide probes attached to a surface, wherein each of said oligonucleotide probes is complementary to a different portion of the mRNA transcribed from said genomic DNA template, and, optionally, to an untranscribed portion of the
20   genomic DNA.

69. The method of paragraph 68, wherein labeled nascent mRNA is harvested at at least three time points during transcription in the presence of a label.

25   70. The method of paragraph 68, wherein said arrangement of oligonucleotide probes comprises
        a) first set of one or more oligonucleotides complementary to the about 200 nt upstream of the 5' end of the transcribed mRNA, comprising at least about three overlapping oligonucleotides that are each about 60-70 nt in length,
30   b) a second set of one or more oligonucleotides complementary to the first about 200 nt of the 5' end of the transcribed mRNA, comprising at least about three overlapping oligonucleotides that are each about 60-70 nt in length,

c) a third set of one or more oligonucleotides complementary to the second about 200 nt of the 5' end of the transcribed mRNA, comprising at least about three overlapping oligonucleotides that are each about 60-70 nt in length, and

d) a fourth set of one or more oligonucleotides complementary to the final about
5   200 nt of a full-length mRNA transcribed from said template, comprising at least about three overlapping oligonucleotides that are each about 60-70 nt in length,.

71. The method of paragraph 70, wherein each set of oligonucleotides is applied together (*e.g.*, spotted together) to the surface.
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72. The method of paragraph 71, wherein each of said oligonucleotides is independently attached to the surface.

73. The method of paragraph 72, wherein the arrangement of oligonucleotides is in the
15   form of a gene chip.

74. The method of paragraph 68, which is high throughput.

75. An arrangement of at least about three addressable oligonucleotide probes attached to
20   a surface, for analyzing mRNA transcription from a DNA template of interest, comprising

a) first set of one or more oligonucleotides complementary to the about 200 nt upstream of the 5' end of the transcribed mRNA, comprising at least about three overlapping oligonucleotides that are each about 60-70 nt in length,

25   b) a second set of one or more oligonucleotides complementary to the first about 200 nt of the 5' end of the transcribed mRNA, comprising at least about three overlapping oligonucleotides that are each about 60-70 nt in length,

c) a third set of one or more oligonucleotides complementary to the second about 200 nt of the 5' end of the transcribed mRNA, comprising at least about three
30   overlapping oligonucleotides that are each about 60-70 nt in length, and

d) a fourth set of one or more oligonucleotides complementary to the final about 200 nt of a full-length mRNA transcribed from said template, comprising at least about three overlapping oligonucleotides that are each about 60-70 nt in length,.

5   76. A method to screen for the presence of a malignancy, immunodeficiency or autoimmunity (including autoimmune damage to a tissue, such as, *e.g.*, kidney, pancreas, brain, gut or liver) in a patient in need thereof, comprising assaying lymphoid tissue of said patient for the presence of an increased level of IGF-1 in the tissue compared to the level in a normal lymphoid tissue.